REMARKS/ARGUMENTS

Claims 1 to 66 are pending in this application. No claims are added, canceled or amended herein.

Applicant's claims are directed to imaging methods that comprise, in part: (a) administering a vitronectin receptor targeted imaging agent and a perfusion imaging agent; and (b) concurrently detecting the vitronectin receptor targeted imaging agent bound at the vitronectin receptor and the perfusion imaging agent. Dependent claims further define the nature of the virtonectin receptor targeted imaging agent, and/or the nature of the perfusion imaging agent. For example, dependent Claim 6 specifies that the vitronectin receptor targeted imaging agent is a diagnostic metallopharmaceutical. Claim 9, which depends from Claim 6, further defines the metallopharmaceutical, specifying that it comprises a metal and a compound, wherein the compound comprises, *inter alia*, a targeting moiety and a chelator capable of chelating the metal. Claim 16, which depends from Claim 9, further specifies that the metal is a radioisotope selected from a recited group of radioisotopes. Claim 19, which depends from Claim 16, specifies that the radioisotope is ^{99m}Tc. Finally, Claim 20, which depends from Claim 19, states that the vitronectin receptor targeted imaging agent may be selected from a group of 19 species of ^{99m}Tc radiopharmaceuticals. Similarly dependent Claims 22, 28, and 42 identify vitronectin receptor targeted imaging agents that may be selected from a group of particular species of radiopharmaceuticals.

In essence, it is asserted in the Office Action that each of the individual species of radiopharmaceuticals set forth in dependent Claims 19, 22, 28, and 42 (except where the species share the same targeting moiety) represents a separate invention, and the Examiner has issued a restriction requirement under 35 U.S.C. § 121 on this basis. Because the Office Action improperly treats what should have been a request for an election of species into an 18-way restriction under Section 121, Applicant respectfully traverses.

Specifically, the Examiner has required restriction under Section 121 between the following Groups:

Group	Claims	Subject Matter[1]	Class
I	1-21, 23-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging agent comprises the sequence, cyclo (Arg-Gly-Asp-Tyr-...Val)	424/1.69
II	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(Arg-Val-Tyr-Asp-...Gly)	424/1.69
III	1-27, 29-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo (Arg-Gly-Asp-Phe-Lys)	424/1.69
IV	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(Arg-Gly-Asp-Tyr-Lys)	424/1.69
V	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, Phe-Glu(cyclo(Lys-Arg-Gly-Asp-Phe)-cyclo (Lys-Arg-Gly-Asp-Nal)	424/1.69
VI	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo (Arg-Gly-Asp-Nal-Lys)	424/1.69
VII	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, Glu (cyclo(Lys-Arg-Gly-Asp-Nal)-cyclo(Lys-Arg-Gly-Asp-Nal)	424/1.69
VIII	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, Glu (O-cyclo (Lys-Arg-Gly-Asp-Phe)-O-cyclo (Lys-Arg-Gly-Asp-Phe)	424/1.69

1 The subject matter of the claim refers to a "targeted imaging agent", not a "target" as stated in the restriction into groups of the office action.

Group	Claims	Subject Matter	Class
IX	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, Glu(O-cyclo(Tyr-aminopropyl)-Val-Arg-Gly-Asp)-O-cyclo(Tyr(3-aminopropyl)-Val-Arg-Gly-Asp)	424/1.69
X	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(Arg-Gly-Asp-Lys(N-5-carbonyl-2-pyridinyl-diazenido)-Val	424/1.69
XI	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(Lys-5-carbonyl-2-pyridinyl-diazendio-Phe-Asp-Gly-Arg	424/1.69
XII	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, 5-carbonyl-2-pyridinyl-diazenido-Glu-cyclo(Lys-Phe-Asp-Gly-Arg)-cyclo(Lys-Phe-Asp-Gly-Arg)	424/1.69
XIII	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(Phe-Lys-5-carbonyl-2-pyridinyl-diazenido-Asp-Gly-Arg	424/1.69
XIV	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(N-Me-Arg-Gly-Asp-ATA-Lys(N-5-carbonyl-2-pyridinyl-diazenido)	424/1.69
XV	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, cyclo(Cit-Gly-Asp-Phe-Lys-5-carbonyl-2-pyridinyl-diazenido)	424/1.69
XVI	1-21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the amino acid sequence, Glu(cyclo-Lys-Arg-Gly-Asp-Phe)-cyclo(Lys-Arg-Gly-Asp-Phe)	424/1.69

Group	Claims	Subject Matter	Class
XVII	1-19, 21-27, 29-41, and 43-66	A method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the compound, Glu-cyclo(Arg-Gly-Asp-Phe-Lys)2-dodecane 1,12-dione	424/1.69
XVIII	1-19, 21, 23-27, 29-41, 43-66	A method of imaging comprising administering a vitronectin receptor target wherein the vitronectin receptor target is not one encompassed in Groups I-XVII above.	424/1.69

It is asserted in the Office Action that the inventions of Groups I to XVIII are unrelated. The Examiner has also required an election of species, from among possible vitronectin targeted imaging agents and possible perfusion agents.

As an initial matter, according to MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05-§ 806.05(i)); ***and***

(B) There must be a serious burden on the examiner if restriction is not required (see MPEP § 803.02, § 806.04(a) - § 806.04(i), § 808.01(a), and § 808.02).

For purposes of the initial requirement, a serious burden may be *prima facie* shown if the examiner shows separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. In the subject application, the Examiner has restricted the claims into 18 different groups. However, ***all 18 groups are classified in Class 424/1.69.*** Thus, Applicant respectfully submit that the Examiner has not established a *prima facie* case of a serious burden.

Moreover, the restriction requirement imposed in the Office Action improperly identifies particular ***species*** that are recited in Markush-type claims, which in turn are further connected by generic linking claims, as separate inventions. Applicant respectfully submits that any restriction among the members of the Markush groups within the claims should only be made provisionally. MPEP § 803.02 which addresses restriction practice with respect to Markush-type claims, clearly sets forth that the Examiner may only require a ***provisional***

election of a single species prior to examination on the merits. The provisional election would be given effect in the event that the Markush-type claim was found not to be allowable. Following election, the Markush-type claim would be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim were not allowable over the prior art, examination would be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration. However, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim would then be extended to the full scope of the generic claims.

The MPEP provides an example in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E. With such a claim, the examiner may require a ***provisional*** election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim is then examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If, on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species would be rejected, and claims to the non-elected species would be held withdrawn from further consideration. On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim would then be extended.

As discussed above, the method comprising administering a vitronectin receptor targeted imaging agent in Claim 1, is referred to in several layers of dependent claims, before finally reaching dependent Claim 20, which sets forth specific examples of ^{99m}Tc radiopharmaceuticals. More than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims within one application. *See* 37 C.F.R. § 1.141. The compounds set forth in dependent Claim 20 are a reasonable number of species of the generic claim 1.

The generic method defined by Claim 1 is a single claimed invention under 35 § U.S.C. 121. The further elements added in dependent Claims 22, 23 to 27, 29 to 41 and 43 to 66 further define the invention set forth in Claim 1. It is respectfully submitted that these

dependent claims, and the groups of compounds set forth therein, do not define independent inventions. The specific radiopharmaceutical compounds set forth in Claim 20 act by the same mode of operation and are each capable of use for the same function. Each of the radiopharmaceutical compounds contains a peptide with a core sequence of Arg-Gly-Asp or Asp-Gly-Arg. The peptides function as targeting moieties for integrins by binding to integrin receptors, for example, the vitronectin receptor. Each of the radiopharmaceutical compounds has the same classification, as acknowledged by the Examiner, in Class 424/1.69. Each of the radiopharmaceutical compounds of Groups I to XVIII provides the same function and acts by the same general mechanism in methods defined by the more generic claims. The mechanism by which these common peptide sequences act as vitronectin receptor targeting agents, finds support in the specification, for example, page 83, l. 25 to p. 84, l. 21.

Thus, Applicant respectfully requests the Examiner to reconsider the restriction requirement, and in particular to consider it only a provisional election of species for the purpose of carrying out the search. Nonetheless, to be fully responsive to the restriction requirement, Applicant elects *with traverse* to prosecute the claims of Group XVI [2]. Further, Applicant elects, *with traverse*, a species where the perfusion imaging agent is Tl-201, as described on page 53, ¶ 59, and the vitronectin receptor targeted imaging agent is the ^{99m}Tc-tricine-TPPTS complex of [[5-[carbonyl]-2-pyridinyl]diazenido]-Phe-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe}, as described in Example 39, page 200.

In view of the above, Applicant respectfully requests that the restriction under 35 U.S.C. § 121 be withdrawn and examination of the application on the merits, on the basis, initially, of the elected species commence. Should the Examiner consider the elected species allowable, consideration of the full generic scope of pending Claims 1 to 22, 23 to 27, 29 to 41 and 43 to 66 is respectfully requested.

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2 Claim 22 should fall within Group XVI since the first radiopharmaceutical of claim 22 is within this group.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (206) 332-1380. Additionally, in the event that the Examiner intends to maintain a restriction under 35 U.S.C. § 121, rather than treat this as a provisional election of species, Applicant proposes an alternative restriction to the following four groups of claims and parenthetically states the relationship to the Examiner's groups:

I. Claims 1-66, drawn to a method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the sequence, Arg-Gly-Asp.
(This encompasses the Examiner's groups I, III, IV, V, VI, VII, VIII, IX, X, XIV, XVI, XVII.)

II. Claims 1-21, 23-27, 29-41, 43-66, drawn to a method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the sequence, Asp-Gly-Arg.
(This encompasses the Examiner's groups XI, XII, XIII.)

III. Claims 1-21, 23-27, 29-41, 43-66, drawn to a method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the sequence, cyclo Arg-D-Val-D-Tyr ... D-Asp-Gly.
(This encompasses the Examiner's group II.)

IV. Claims 1-21, 23-41, 43-66, drawn to a method of imaging comprising administering a vitronectin receptor targeted imaging agent wherein the targeted imaging comprises the sequence, cyclo Cit-Gly-Asp-D-Phe-Lys -5-carbonyl-2-pyridinyl-diazenido.
(This encompasses the Examiner's group XV.)

The proposed four groupings of claims are based on the amino acid sequence of the binding domain found on vitronectin for the vitronectin receptor, e.g., Arg-Gly-Asp, and variations thereof, Asp-Gly-Arg.

Date: May 12, 2003

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